

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

**In re Application of:**

Houtzager et al.

**Serial No.:** To be assigned

**Filed:** December 10, 2001

**For:** A STRUCTURE FOR PRESENTING  
DESIRED PEPTIDE SEQUENCES

**Examiner:** To be assigned

**Group Art Unit:** To be assigned

**Attorney Docket No.:** 2183-5208US

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**PRELIMINARY AMENDMENT**

Commissioner for Patents  
Washington, D.C. 20231

Sir:

Prior to examination of the above-referenced patent application on the merits, entry of the amendments as set forth herein is respectfully solicited.

**IN THE CLAIMS:**

Please amend claims as follows. Please note that claim amendments are presented here in clean form for clarity, a marked up version of the claim amendments is attached.

1. A synthetic or recombinant proteinaceous molecule comprising:  
a core comprising a b-barrel, wherein said b-barrel comprises at least four strands and at least two b-sheets, wherein each of said b-sheets comprises two of said strands; and  
a binding peptide comprising a peptide connecting two strands in said b-barrel and wherein said binding peptide is outside its natural context.

2. The proteinaceous molecule of claim 1, wherein said b-barrel comprises at least five strands, and wherein at least one of said sheets comprises three of said strands.

3. (Amended) The proteinaceous molecule of claim 1, wherein said b-barrel comprises at least six strands, and wherein at least two of said sheets comprises three of said strands.

4. (Amended) The proteinaceous molecule of claim 1, wherein said b-barrel comprises at least seven strands, and wherein at least one of said sheets comprises 4 of said strands.

5. (Amended) The proteinaceous molecule of claim 1, wherein said b-barrel comprises at least eight strands, and wherein at least one of said sheets comprises four of said strands.

6. (Amended) The proteinaceous molecule of claim 1, wherein said b-barrel comprises at least nine strands, and wherein at least one of said sheets comprises four of said strands.

7. (Amended) The proteinaceous molecule of claim 1, wherein said binding peptide connects two strands of said b-barrel on the open side of said barrel.

8. (Amended) The proteinaceous molecule of claim 1, wherein said binding peptide connects said at least two b-sheets of said barrel.

9. (Amended) The proteinaceous molecule of claim 1, further comprising at least one further binding peptide.

10. (Amended) The proteinaceous molecule of claim 1, further comprising three binding peptides and three connecting peptide sequences.

11. (Amended) The proteinaceous molecule of claim 1, further comprising at least four binding peptides.

12. The proteinaceous molecule of claim 11, wherein at least one binding peptide recognizes a target molecule that is different than at least one of the other binding peptides.

13. (Amended) A process for identifying a proteinaceous molecule with an altered binding property, said process comprising:  
introducing an alteration in the core of the proteinaceous molecules of claim 1; and  
selecting a proteinaceous molecule with an altered binding property from said proteinaceous molecules.

14. (Amended) A process for identifying a proteinaceous molecule with an altered structural property, said process comprising:  
introducing an alteration in the core of the proteinaceous molecules of claim 1; and  
selecting a proteinaceous molecule with an altered binding property from said proteinaceous molecules.

15. (Amended) The process of claim 13, wherein said alteration comprises a post-translational modification.

16. (Amended) The process of claim 13, wherein said alteration is introduced into a nucleic acid coding for said at least one proteinaceous molecule, the method further comprising: expressing said nucleic acid in an expression system that is capable of producing said proteinaceous molecule.

17. (Amended) The proteinaceous molecule produced by the process of claim 13.

18. (Amended) The proteinaceous molecule of claims 1, wherein said proteinaceous molecule is derived from the immunoglobulin superfamily.

19. The proteinaceous molecule of claim 18, wherein the exterior of the proteinaceous molecule is immunologically similar to said immunoglobulin superfamily molecule it was derived from.

20. (Amended) A cell comprising a proteinaceous molecule of claim 1.

21. A method for producing a nucleic acid encoding a proteinaceous molecule capable of displaying at least one desired peptide sequence comprising: providing a nucleic acid sequence encoding at least a first structural region and a second structural region separated by a nucleic acid sequence encoding said desired peptide sequence or a region where such a sequence can be inserted; and mutating said nucleic acid encoding said first and said second structural regions to obtain a desired nucleic acid encoding said proteinaceous molecule capable of displaying at least one desired peptide sequence.

22. A method for displaying a desired peptide sequence, comprising:  
providing a nucleic acid comprising a region for inserting a sequence encoding said desired peptide sequence, wherein said nucleic acid further encodes at least two b-sheets, wherein said at least two b-sheets form a b-barrel;  
inserting a nucleic acid sequence comprising said desired peptide sequence into said region; and  
expressing said nucleic acid such that said at least two b-sheets are obtainable by the method according to claim 21.

23. (Amended) A method of separating a substance from a mixture, comprising:  
mixing a proteinaceous substance comprising the proteinaceous molecule of claim 1, wherein said proteinaceous substance binds to said substance; and  
separating said substance from said mixture.

24. The method according to claim 23, wherein said mixture comprises a biological fluid.

25. The method according to claim 24, wherein said biological fluid comprises an excretion product of an organism.

26. The method according to claim 25, wherein said excretion product comprises milk or a derivative of milk.

27. The method according to claim 24, wherein said mixture is blood or a derivative thereof.

28. (Amended) A pharmaceutical composition comprising the proteinaceous molecule of claim 1 and a pharmaceutically acceptable substrate.

29. (Amended) A method of treating a pathological condition involving unwanted proteins, cells, or microorganisms, said method comprising:  
administering a pharmaceutical composition comprising the proteinaceous molecule of claim 1 in a pharmaceutically acceptable manner in a pharmaceutically effective amount.

30. (Amended) A method of detecting molecules in a diagnostic assay, comprising:  
detecting said molecules using an effective of a proteinaceous substance comprising the proteinaceous molecule of claim 1.

31. (Amended) A gene delivery vehicle comprising:  
the proteinaceous molecule of claim 1; and  
a gene of interest.

32. (Amended) A gene delivery vehicle comprising:  
a nucleic acid encoding the proteinaceous molecule of claim 1; and  
a nucleic acid encoding a gene of interest.

33. (Amended) The proteinaceous molecule of claim 1 conjugated to a moiety of interest.

34. The proteinaceous molecule of claim 33, where said moiety of interest is a toxic moiety.

35. (Amended) A chromatography column comprising:  
the proteinaceous molecule of claim 1; and  
a packing material.

36. A nucleic acid produced by the method according to claim 21.

37. A nucleic acid library comprising a collection of different nucleic acids produced by the method according to claim 36.

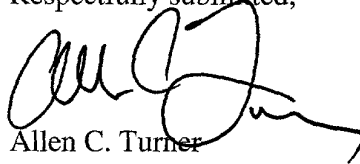
38. The nucleic acid library of claim 37, further comprising a collection of nucleic acids encoding different affinity regions.

39. (Amended) The nucleic acid library of claim 37, wherein said nucleic acid library is an expression library

**REMARKS**

No new matter has been added. The Applicants again request entry of the amendments as set forth in the Appendices hereto prior to examination of the application on the merits.

Respectfully submitted,



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ACT/bv



**VERSION OF CLAIMS WITH MARKINGS TO SHOW CHANGES MADE**

1. A synthetic or recombinant proteinaceous molecule comprising:  
a core comprising a b-barrel, wherein said b-barrel comprises at least four strands and at least two b-sheets, wherein each of said b-sheets comprises two of said strands; and  
a binding peptide comprising a peptide connecting two strands in said b-barrel and wherein said binding peptide is outside its natural context.
2. The proteinaceous molecule of claim 1, wherein said b-barrel comprises at least five strands, and wherein at least one of said sheets comprises three of said strands.
3. The proteinaceous molecule of claim 1 [or claim 2], wherein said b-barrel comprises at least six strands, and wherein at least two of said sheets comprises three of said strands.
4. The proteinaceous molecule of claim 1, [claim 2, or claim 3,] wherein said b-barrel comprises at least seven strands, and wherein at least one of said sheets comprises 4 of said strands.
5. The proteinaceous molecule of claim 1, [claim 2, claim 3, or claim 4,] wherein said b-barrel comprises at least eight strands, and wherein at least one of said sheets comprises four of said strands.
6. The proteinaceous molecule of [any one of] claim[s] 1[-5], wherein said b-barrel comprises at least nine strands, and wherein at least one of said sheets comprises four of said strands.

7. The proteinaceous molecule of [any one of] claim[s] 1[-6], wherein said binding peptide connects two strands of said b-barrel on the open side of said barrel.

8. The proteinaceous molecule of [any one of] claim[s] 1[-7], wherein said binding peptide connects said at least two b-sheets of said barrel.

9. The proteinaceous molecule of [any one of] claim[s] 1[-8], further comprising at least one further binding peptide.

10. The proteinaceous molecule of [any one of] claim[s] 1[-9], further comprising three binding peptides and three connecting peptide sequences.

11. The proteinaceous molecule of [any one of] claim[s] 1[-9], further comprising at least four binding peptides.

12. The proteinaceous molecule of claim 11, wherein at least one binding peptide recognizes a target molecule that is different than at least one of the other binding peptides.

13. A process for identifying a proteinaceous molecule with an altered binding property, said process comprising:  
introducing an alteration in the core of the proteinaceous molecules of [any one of] claim[s] 1[-12]; and  
selecting a proteinaceous molecule with an altered binding property from said proteinaceous molecules.

14. A process for identifying a proteinaceous molecule with an altered structural property, said process comprising:

introducing an alteration in the core of the proteinaceous molecules of [any one of] claim[s] 1[-12]; and  
selecting a proteinaceous molecule with an altered binding property from said proteinaceous molecules.

15. The process of claim 13 [or claim 14], wherein said alteration comprises a post-translational modification.

16. The process of claim 13, [claim 14, or claim 15,] wherein said alteration is introduced into a nucleic acid coding for said at least one proteinaceous molecule, the method further comprising:  
expressing said nucleic acid in an expression system that is capable of producing said proteinaceous molecule.

17. The proteinaceous molecule produced by the process[es] of claim 13[, claim 14, claim 15, or claim 16].

18. The proteinaceous molecule of [any one of] claims 1[-12 or 17], wherein said proteinaceous molecule is derived from the immunoglobulin superfamily.

19. The proteinaceous molecule of claim 18, wherein the exterior of the proteinaceous molecule is immunologically similar to said immunoglobulin superfamily molecule it was derived from.

20. A cell comprising a proteinaceous molecule of [any one of] claim[s] 1[-12 or 17-19].

21. A method for producing a nucleic acid encoding a proteinaceous molecule capable of displaying at least one desired peptide sequence comprising:  
providing a nucleic acid sequence encoding at least a first structural region and a second structural region separated by a nucleic acid sequence encoding said desired peptide sequence or a region where such a sequence can be inserted; and  
mutating said nucleic acid encoding said first and said second structural regions to obtain a desired nucleic acid encoding said proteinaceous molecule capable of displaying at least one desired peptide sequence.

22. A method for displaying a desired peptide sequence, comprising:  
providing a nucleic acid comprising a region for inserting a sequence encoding said desired peptide sequence, wherein said nucleic acid further encodes at least two b-sheets, wherein said at least two b-sheets form a b-barrel;  
inserting a nucleic acid sequence comprising said desired peptide sequence into said region; and  
expressing said nucleic acid such that said at least two b-sheets are obtainable by the method according to claim 21.

23. A method of separating a substance from a mixture, comprising:  
mixing a proteinaceous substance comprising the proteinaceous molecule of [any one of] claim[s] 1[-12 or 17-19], wherein said proteinaceous substance binds to said substance; and  
separating said substance from said mixture.

24. The method according to claim 23, wherein said mixture comprises a biological fluid.

25. The method according to claim 24, wherein said biological fluid comprises an excretion product of an organism.
26. The method according to claim 25, wherein said excretion product comprises milk or a derivative of milk.
27. The method according to claim 24, wherein said mixture is blood or a derivative thereof.
28. A pharmaceutical composition comprising the proteinaceous molecule of [any one of] claim[s] 1[-12 or 17-19] and a pharmaceutically acceptable substrate.
29. A method of treating a pathological condition involving unwanted proteins, cells, or microorganisms, said method comprising:  
administering a pharmaceutical composition comprising the proteinaceous molecule of [any one of] claim[s] 1[-12 or 17-19] in a pharmaceutically acceptable manner in a pharmaceutically effective amount.
30. A method of detecting molecules in a diagnostic assay, comprising:  
detecting said molecules using an effective of a proteinaceous substance comprising the proteinaceous molecule of [any one of] claim[s] 1[-12 or 17-19].
31. A gene delivery vehicle comprising:  
the proteinaceous molecule of [any one of] claim[s] 1[-12 or 17-19]; and  
a gene of interest.

32. A gene delivery vehicle comprising:  
a nucleic acid encoding the proteinaceous molecule of [any one of] claim[s] 1[-12 or 17-19]; and  
a nucleic acid encoding a gene of interest.

33. The proteinaceous molecule of [any one of] claim[s] 1[-12 or 17-19] conjugated  
to a moiety of interest.

34. The proteinaceous molecule of claim 33, where said moiety of interest is a toxic  
moiety.

35. A chromatography column comprising:  
the proteinaceous molecule of [any one of] claim[s] 1[-12 or 17-19]; and  
a packing material.

36. A nucleic acid produced by the method according to claim 21.

37. A nucleic acid library comprising a collection of different nucleic acids produced  
by the method according to claim 36.

38. The nucleic acid library of claim 37, further comprising a collection of nucleic  
acids encoding different affinity regions.

39. The nucleic acid library of claim 37 [or claim 38], wherein said nucleic acid  
library is an expression library.